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Examiner: **DRODGE, Joseph W.**

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Translation of the Swedish Patent Application No. 9903841-6

VERIFICATION OF TRANSLATION

I, Bengt Söderström of Försvarets Materielverk, SE-115 88 Stockholm, do hereby solemnly and sincerely declare that I am conversant with the English and Swedish languages, and that the following translation made by me of the specification, claims and abstract of the Swedish Patent Application No. 9903841-6 as filed on October 26, 1999 is true to the best of my knowledge and belief.

Stockholm April 22, 2002

Bengt Söderström

Method and apparatus for processing blood and blood components (Branched off from the Swedish patent application 9901980-4)

The claimed invention relates to a method and an apparatus for pre-processing blood concentrate products before they are exposed to continued processing for extracting those remaining subcomponents that are of interest. The pre-processing of blood concentrate products, primarily pertaining to the invention, entails a resolution of these in a diluting solution and a flushing of the containers or bags in which the blood concentrate products are delivered. This makes possible the subsequent processing operation in the form of centrifuging and dividing up of blood concentrate products into blood-platelet plasma and waste products.

The invention is primarily intended for pre-processing of such blood concentrate products that are designated "Buffy Coat" at blood-donor centres and which are obtained when red blood cells and plasma are separated from whole blood and which at present are utilised for extracting valuable medicinal blood-platelet plasma. At this stage the Buffy Coat is a thick viscous liquid that must be resolved in a suitable diluting solution before it can be exposed to renewed centrifugation. An example of such a standardised diluting solution, which widely used, is a product commonly named T-Sol. In normal cases the Buffy coat is accessible in the form of concentrate from the previous extraction of red blood cells and plasma from whole blood. Each concentrate batch of Buffy Coat is, as a rule, too small to be worth an individual centrifuging after resolution in the current diluting solution. As every Buffy Coat concentrate is initially accessible in its own blood processing bag, a fixed amount of diluting solution was previously added manually to each one of a number of blood processing bags and shaken manually until an acceptable mixing had taken place, followed by emptying them together into a larger bag which was then centrifuged. Apart from all manual handling and the time required for this there is also the added risk to the person who must shake the blood bags and in the long term can receive injury to the neck and shoulders.

To be able to also automate this stage in blood processing it is suggested, in accordance with the claimed invention, the use of a specially intended set of bags preferably containing a ring-shaped bag for the following centrifuging operation as well as the use of a characteristic automatic mixing device, special to the invention, in which the Buffy coat is added and resolved in a diluting solution. In the preferred design of this part of the invention, the mixing function or the mixing device has been built into or made connectable to the outer lid of the centrifuge that is utilised

in the processing stage that follows after. Nevertheless, the device can also be made to stand completely by itself without changing the original concept. In the device, in accordance with the invention, a smaller electrically driven motor is thus included which, when the device is combined with the centrifuge, is secured to the lid of the centrifuge. This motor has the distinct feature of never doing a complete revolution in any direction but is quickly stopped before a revolution is completed then followed by an incomplete revolution in the opposite direction. A movement of approximately one quarter of a revolution (such as +92°), lasting one or several minutes, has shown that it gives the desired mixing function, which, as will become evident, has as its task the replacement of the prior manual resolution of the Buffy Coat and the flushing out of the Buffy Coat bags with the required amount of diluting solution, which procedure today generally precedes the so called Pooling, in other words, the merging of several flushed out quantities of concentrate products to form a suitable batch for centrifugation. The device's special movement pattern can be attained with a gearbox, a crank function or via the control of its motor. From a theoretical point of view a hydraulic motor could also be used for this purpose, even when taking into account a lower shaking speed and longer mixing time. Connected to the aforementioned motor there is a cassette or holder in which the number of concentrate bags with Buffy Coat intended to be included in a process can be attached. Before the concentrate bags are attached to the cassette they have been connected to the bag set intended for processing, via individual connecting tubes, by sterile welding and which bag set also contains a connecting tube with which all bags containing Buffy Coat can be connected to a bag with the required amount of diluting solution, as well as a second connecting tube to the ring bag intended for the finishing centrifugation and finally a connecting tube between the ring bag and a storage bag for the desired final product. Together these components make up a functionally sealed system, which is easy to handle, and completely protected against external bacteria, etc.

When extracting blood platelet plasma from the Buffy Coat the number of bags with starting material that are intended to be included in a centrifugation are connected to individual connecting tubes in the aforementioned bag set. These connecting tubes are then in turn joined in a multi-way connector to which the connecting tube form the diluting solution bag is also connected. The latter connecting tube is at the same time attached to a clamp valve while the bags with Buffy Coat are secured to the aforementioned cassette and the bag with the diluting solution is suspended in the intended holder sufficiently high up to allow the desired amount of diluting solution to be transferred to each respective Buffy Coat bag. The addition of the

diluting solution to the Buffy Coat bags is then controlled by a clamp valve, which, in turn, is controlled by a control program that can be included in the control program of the control system of the centrifuge and which control program also selects the time to start the motor and the time it must be operated. Appropriately, the diluting solution is added in several portions with a motor driven action between each addition. Dissolving the Buffy Coat in the diluting solution is thus carried out without any manual shaking operation. Due to the special timed movement, back and forth, of the motor the problem of damaging the various tubes is avoided. It is only the ring bag and the tube between it and the end-product storage bag that are not affected by the mixing operation. After the dissolution of the Buffy Coat in the different original bags is finalised the contents of all bags are added to the ring bag included in the bag set via a separate connecting tube, which also is connected to the previously named multi-way connector and which on its way to the ring bag is passing a clamp valve by which this connection is controlled. After all substance has been transferred to the ring bag the connection is interrupted between the ring bag and the original bags and the diluting solution bag by cutting the relevant connecting tube by welding in the centrifuge rotor´s support which it passes, after which the empty bags and their connecting tubes can be rejected. Following this the diluting solution/Buffy Coat mix is centrifuged while the bag intended for storing the end product is located in the centre chamber of the centrifuge rotor. After centrifugation the lighter blood platelet product is transferred to the final storage bag. In this connection a known device is utilised for exposing the ring bag to an external pressure thus emptying it to a greater or lesser degree. This device consists of a membrane arranged under the ring bag, beneath which hydraulic fluid can be added in order to expose the ring bag to an external pressure. The interruption of the emptying of the ring bag is controlled by one or more photocells in the outer lid of the centrifuge, which photocells utilise the difference in colour between the light desired platelet-rich end product and the dark heavier residue products that are gathered along the outer periphery of the bag. When emptying the ring bag it is suitable to do this via a cell trap, which can, for example, be of the type described in WO 97/30715. After the desired amount of blood-platelet plasma has been removed from the ring bag the connecting tube from the ring bag to the final storage bag is cut by welding in a known way, whereby both the so formed ends of the tube are blocked. All that remains after that is to point out that the holder for the diluting solution bag and the cassette for the Buffy Coat bags can be made removable in order not to interfere with the other functions of the centrifuge.

The invention in its various functions has now been defined in the subsequent patent claims and they shall now only be somewhat more described in relation to the attached figures.

Of these

Fig. 1 shows a bag set intended for blood-platelet production from Buffy Coat

Fig. 2 shows an angle projection of a centrifuge equipped for autopooling in accordance with the invention.

The bag set shown in Fig. 1 for blood-platelet production from Buffy Coat comprises a ring bag 22, a bag for diluting solution 23, four connecting tubes 25-28 (the number of connecting tubes can vary but should as a rule be between 4 and 6), each one of which is intended for welding to a Buffy Coat bag, a multi-way connector 29, which, on the one hand, is connected via tube 30 to the diluting solution bag 23 and, on the other hand, via another tube 31 to the ring bag 22. From the latter a further tube 32 is connected to a final storage bag 33. In the tube 30 connection to the diluting solution bag 23 there is a breaker switch 45, which can be opened by sharply bending the tube when addition of diluting solution to the Buffy Coat bag connected to the tubes 25-28 is required. Before the breaker switch is opened the connecting tube 30 must be engaged in the guide groove 12 in one of the supports 9-11 with which the clamp valve function is intended to control the addition of diluting solution.

As the bag set shown in Fig 1 is the same as illustrated in Figure 2 we have retained the same designations although the parts are drawn to a smaller scale and consequently also with fewer details. Otherwise, in Fig. 2, a centrifuge 34 is shown standing with its outer lid 35 completely open and locked in position. The inner lid of the centrifuge has been omitted in the figure as it made the figure unclear when drawn in position. Also the centrifuge rotor and the ring bag 22 have been drawn, to a certain extent, in a simplified way. The control panel of the centrifuge is numbered 36 in the figure. Furthermore, the figure shows a situation with four blood bags containing Buffy Coat 37-40 suspended in a cassette 41, which is mounted on the outer lid of the centrifuge. The respective outlets of blood bags 37-40 have, by sterile welding, been joined to the connecting tubes 25-28 and the fluid content of the bags has been transferred to the ring bag 22 via these tubes and the connecting tube 31. After that, the bags 37-40 have received cleaning and diluting fluid from the diluting fluid bag 23 suspended in the holder 44. The diluting fluid bag

23 is suspended sufficiently high above the bags 37-40 to enable the diluting solution, in sufficient amounts, to be added to these bags as soon as the breaker switch 45 in the tube 30 and the clamp valve in the support 11, which tube 30 passes, is opened. The communication between the bags 37-40 and the ring bag 22 is via the tube 31, which, in turn, passes the clamp valve in the support 10 by which communication is controlled. After the addition of diluting solution in sufficient amounts to the bags 37-40, the motor connected to the cassette starts (not seen on the figure) and operates cassette 41 forwards and backwards in a pendulum movement, in accordance with curve 42, until all concentrate substance in the Buffy Coat bags has dissolved, after which the built-in clamp valve in the support 10 opens up, through which clamp valve outlet tube 31 from the multi-way connector 29 passes, and all substance is added to the ring bag 22 after which the tube 31, in the support 10, is sterile welded and blocked whereby the empty bags 37-40 and the bag 23 with possible rests of diluting solution can be rejected together with the tube system. Flushing out of the blood bags can, if necessary, be carried out as two or several consecutive flushing stages. After completed flushing of the blood bags the cassette 41 and the holder 44 are removed from the centrifuge lid and the centrifuge is closed and the centrifugation is carried out. The final storage bag 33 is located in the centre chamber 45 of the centrifuge. After centrifugation all blood-platelet plasma is transferred to the final storage bag 33 by supplying hydraulic fluid to the chamber 5 under the ring bag and thereby exposing the ring bag to an external pressure, which presses it together. The emptying of the ring bag is interrupted by the photocell 52 when it registers that the interface between the desired lighter substance and the darker non-desired concentrate product starts to reach the outlet via tube 32. Following this, the tube 32 is cut and sealed by sterile welding in one of the supports 9-11, after which the ring bag with the non-desired residues of red blood cells, etc. can be rejected.

Claims:

1. Method of pre-processing blood concentrate products from a previous centrifugation of whole blood before these concentrate products are exposed to yet an other centrifugation for separating recoverable, still accessible, medicinally valuable components, *characterised in that* a number of bags (37-40) containing blood concentrate products to be included in the current new centrifugation are connected to a multi-way connector by means of individual outlet tubes (25-28) from the bags, and that a supply tube (30) from a bag (23) containing a diluting solution is also connected to said multi-way connector, after which the bags (37-40) containing blood concentrate products are suspended in a cassette (41), which is capable of being operated forwards and backwards in incomplete pendulum swings (42) by a motor adapted to the cassette, and that diluting solution is added in adapted portions to the bags (37-40) containing concentrate products from the bag (23) containing the diluting solution, and that the cassette (41) is kept in motion by the motor until all concentrate products are dissolved in the added diluting solution, after which the contents of all bags in the cassette are transferred to a new bag (22) for the subsequent centrifugation.

2. Method according to claim 1, *characterised in that* the amount of diluting solution added to each respective bag is controlled by a clamp valve (11) through which the supply tube (30) for diluting solution passes, and which clamp valve can also be utilised for cutting the tube by welding when processing is finalised.

3. Method according to claim 1 or 2, *characterised in that* the pendulum movement of the cassette (41) is kept within plus/minus approximately a quarter of a revolution.

4. Method according to any one of claims 1-3, *characterised in that* after the addition of and treatment with diluting solution, the contents of all bags containing concentrate products (37-40) are transferred, via a tube connected to the same multi-way connector (29) as the other tubes, to a ring-bag (22) in which the subsequent centrifugation is carried out.

5. Method according to any one of claims 1-4, *characterised in that* the addition of diluting solution and the transfer of dissolved concentrate products are made in several steps with mixing steps between said steps.

6. Device for carrying out the method according to any one of claims 1-5, characterised in that it comprises a cassette (41) in which a number of standard bags containing blood concentrate products from a previous centrifugation can be suspended and in which they can be connected, via a multi-way valve (29), to a source (23) for controlled supply of diluting fluid, and that the cassette (41) can be operated, by a motor adapted to said cassette, in a forward and backward pendulum movement consisting only of incomplete revolutions around an axis.

7. Device according to claim 6, characterised in that it further comprises attachment means for a container or bag containing diluting fluid, which via a control valve is connected to the same multi-way connector (29) as the bags containing blood concentrate products.

8. Device according to claim 6 or 7, characterised in that the pendulum movement of the motor being within the interval plus/minus approximately a quarter of a revolution.

9. Bag-set for processing blood concentrate products according to the method of any one of claims 1-4 and/or the device according to any one of claims 6-8, characterised in that it comprises a ring-bag (22); a bag (23) containing diluting solution; more than two connecting tubes (25-28), each one of which is intended to be connected to a bag containing blood concentrate products, and a multi-way connector (29), and that said connecting tubes, said bag (23) containing diluting solution and said ring-bag (22) are all connected to the multi-way connector, where they can be put in fluid communication with each other while a final storage bag (33) is separately connected to the ring-bag.

10. Centrifuge for carrying out the method according to any one of the claims 1-5, characterised in that it comprises a motor function, disposed in its outer lid (35), having the most distinctive feature of making, when activated, an incomplete revolution (42) immediately followed by a corresponding incomplete return revolution to and past the point of departure, and that said motor function can be combined with a holder or cassette (41) in which a number of blood bags (37-40) can be suspended, when the outer lid of the centrifuge is fully open, in order to expose the substance in said bags for a mechanical mixing when the motor is activated.

Summary

The claimed invention relates to a method and a device for processing blood concentrate products before they are exposed to a continued process for extracting remaining medicinally interesting sub-components. The appropriate pre-processing according to the invention primarily entails a mechanically powered resolution of the viscous flowing concentrate products in a diluting solution for adapting the added-together product for a renewed centrifugation.